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Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active. Cancer Screening During the Coronavirus Disease-2019 Pandemic: A Perspective From the National Cancer Institute's PROSPR Consortium

he severe acute respiratory syndrome novel coronavirus-2 (SARS-CoV-2) virus pandemic and related coronavirus disease (COVID-19), have dramatically altered health care delivery, worsened non-virusrelated health outcomes, and increased the potential for disparities. As COVID-19 infections increased, public health and professional organizations issued guidance that all nonurgent surgeries and procedures, including cancer screening, should be delayed.<sup>1</sup> Not surprisingly, early data suggest that these restrictions drastically impacted preventive care that requires direct patient-provider contact. Even for conditions requiring urgent intervention, such as myocardial infarctions,<sup>2</sup> there is evidence that patients recently decreased health care use. An online evaluation by the EPIC health research network suggested fewer cancer screening encounters during the pandemic: however, these analyses did not directly measure recommended cancer screening tests within age-eligible populations and did not examine disparities over time.<sup>3</sup> Thus, the pandemic's broader impact on commonly performed cancer prevention and control measures remains largely unknown.

Decreases in cancer screening are particularly alarming because routinely screening asymptomatic people decreases morbidity and mortality related to breast, cervical, colorectal, and lung cancers.<sup>4</sup> The current US Preventive Services Task Force recommendations include: biennial breast cancer screening with mammography in women ages 50-74 years; annual lung screening with lowdose computed tomography in adults aged 55-80 years with a >30 packyear smoking history and a quit date within 15 years; colorectal cancer screening, most commonly completed using annual fecal immunochemical testing (FIT) or colonoscopy every 10 years among average risk adults aged 50-75 years; and periodic cervical screening with cytology with or without human papillomavirus testing in women ages 21-65 years.<sup>4</sup> Thus, almost every adult is recommended to receive multiple cancer screening tests during their lifetime. At present, minimal data are available regarding the pandemic's impact on cancer screening between diverse health care settings, among different cancer types, by various screening tests, and across disparate demographic groups.

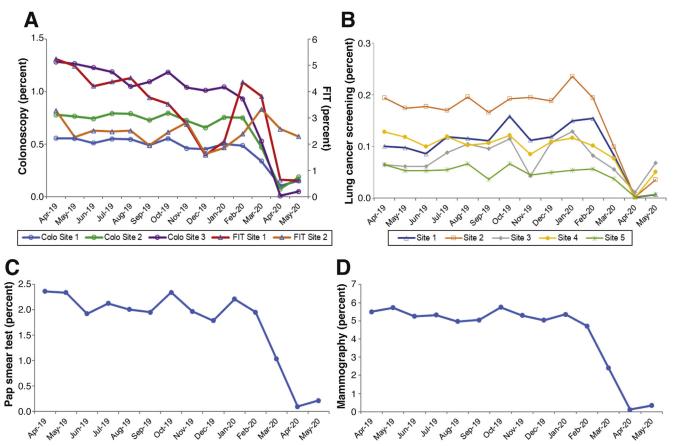
To address these knowledge gaps and to formulate a roadmap for resuming cancer screening, the National Cancer Institute's Populationbased Research to Optimize the Screening Process (PROSPR) consortium compared breast, cervical, colorectal, and lung cancer screening rates before and after the pandemic and developed pragmatic recommendations. The PROSPR consortium is designed to evaluate and improve cancer screening processes and outcomes. Data were available from eight large health care systems in seven states, covering >11 million individuals (approximately 1 of every 30 people in the United States). Most sites studied rapidly approached zero popscreening among target-age ulations during the early phase of the pandemic, across diverse types of health care delivery systems (Figure 1). Breast cancer screening had the largest decrease (a 96% decrease), from 5.3% of age-eligible persons screened per month in April to September 2019 to 0.23% in April and May 2020 (P < .01). Screening for lung, cervical, and colorectal cancers at most sites had similar declines with 62%. 92%, and 82% decreases, respectively.

Two important findings may inform future actions. First, 1 large site in the

Western United States continued mailing FIT for colorectal screening, which does not require a face-to-face interaction, and maintained high screening test returns during April and May 2020 (Figure 1; tests are sent steadily over the year related to birthday, for members not up to date with screening. Typical FIT return rates are >50% and the net screening up-to-date proportion for this site, using all modalities, is >80% (this includes people with a prior colonoscopy for FIT positive). This notable exception strongly suggests that remote cancer screening methods can be successful during the pandemic. Although remote sampling methods, such as FIT or human papilloma virus testing, allow widespread testing without inperson contacts for initial screening, they still require follow-up in-person evaluations for positive tests. This point emphasizes the need for safe inperson testing environments. Second, screening decreases were uniform sites. despite marked across geographical variation in underlying SARS-CoV-2 infection rates: around May 10, for example, the 7-day average test positivity rates for states with PROSPR centers studied ranged from 0.3% to 16.8%, even though almost all sites approached zero screening. This discordance suggests the potential for closer alignment between local infection risk and concomitant reductions in preventive health care delivery, assuming ample SARS-CoV-2 monitoring is available. Positive testing rates for SARS-CoV-2 are difficult to interpret, given variation in testing criteria during the pandemic (eg, symptomatic vs asymptomatic). The infection rates for preprocedure testing of asymptomatic people are likelv far lower.<sup>5</sup>

The costs of decreasing cancer screening are likely to include delayed cancer detection, more advanced stages of malignancy at diagnosis, and loss of life-years among those with cancer. A modeling study from the National Cancer Institute's Cancer Intervention and Surveillance Modeling Network suggested that even moderately longer times between a

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**Figure 1.**Changes in cancer screening rates among screening eligible ages (by cancer type) within 8 PROSPR sites. Five PROSPR sites contributed to lung cancer data for low-dose computerized tomography (LDCT), 3 sites to colorectal cancer data, 1 to breast cancer data, and 1 to cervical cancer data. Two colorectal cancer sites provided data for both total colonoscopies performed and fecal immunochemical testing (FIT) completed. Variations in FIT-based screening also relate to site-specific variations in outreach during holiday periods (less outreach) and colon cancer awareness month. Lung cancer data include screening eligible ages, but do not include smoking history criteria.

positive screening test and follow-up diagnostic testing could significantly reduce the life-years gained from cancer screening.<sup>6</sup> Significantly decreased benefit was suggested with even a few weeks delay for breast cancer and within months for colorectal cancer.<sup>6</sup> The decreases in screening across the States demonstrated United bv PROSPR data predict substantial increases in cancer morbidity and mortality in the coming years. Although detailed cancer diagnoses, staging, and survival during the pandemic await verification from cancer registries, 1 PROSPR site with such real-time pathology data demonstrated that the monthly average colorectal cancer diagnoses decreased by 31% between April and September 2019 and April and May 2020 (P < .01).

Still unknown is whether pandemic-related health care changes will induce disparities in other health outcomes, including cancers amenable to screening.<sup>7</sup> This uncertainty is despite well-documented racial, ethnic, and socioeconomic disparities for COVID-related diagnoses and deaths.<sup>8,9</sup> Among persons completing screening within the PROSPR populations studied, screening rates decreased markedly across all PROSPR sites, for all cancer types, independent of race/ ethnicity (P > .10 for all comparisons). Among persons screened, the demographic proportions completing a test were similar before versus during the COVID-19 pandemic by race/ ethnicity (eg, non-Hispanic Whites 50% vs 46%; Hispanic 22% vs 29%; Asian 16% vs 13%; and African Americans 7% vs 8%, respectively).

The reintroduction of cancer screening during the pandemic, however, poses a large risk for enhancing or introducing new disparities. Will the COVID-19–related financial stresses on

health care systems allow equal resumption of robust screening programs across the population? Will shifts to telemedicine generate differences in who will request or be referred for screening, who will receive and complete active outreach, or who will schedule in-person followup testing? Will the pandemic's economic ramifications (which impact job and insurance status) exacerbate existing national sociodemographic differences in health care access and outcomes? The resumption of routine health care practices, including cancer screening, must incorporate intentional strategies to minimize the introduction of health disparities.

We urgently recommend several pragmatic steps to address the opportunities and challenges of resuming cancer screening services during the pandemic. Informed by the data presented, and with the goal of increasing

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effective, consistent, and universal delivery of safe screening services, the PROSPR consortium has developed and recommends the following urgent interventions:

- Broader implementation of remote testing, to reduce the need for in person visits, such as increased use of established methods (eg, mailed FIT for colorectal cancer screening) and rapid evaluation of emerging strategies (eg, self-sampling for human papillomavirus for cervical cancer screening).
- Screening outreach programs that intentionally target patients at highest <u>social</u> risk, including demographic groups who are less likely to spontaneously seek or complete screening.
- Rapid implementation of risk stratification tools to identify those at highest <u>medical</u> risk of cancer by age and other risk factors (including lack of prior screening) and those at lowest risk, who are unlikely to benefit from screening.
- Infection control measures to maximize patients and staff safety, such as pre-procedure testing. These measures should include effective communication to decrease patient concerns regarding screening. Test performance characteristics (ie, false positives and negatives) will influence the benefit of preprocedure testing at very low or moderately high background levels of disease prevalence.<sup>5</sup>
- Customized cancer screening practices, coordinated with local SARS-CoV-2 risk, to maximize screening test completion in areas with low viral prevalence.
- Real-time demographic data for early identification of screening service uptake disparities.

The COVID-19 pandemic has created unprecedented decreases in cancer screening services, which will likely have long-term deleterious effects on cancer morbidity and mortality. When to resume routine care remains uncertain and delivery patterns may change. Several pragmatic steps are urgently recommended to reduce potential cancer-related outcomes and to avoid exacerbating disparities. These steps can help to restart screening and thereby equitably decrease the noninfectious impacts of the SARS-CoV-2 pandemic.

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